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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY DOCKET NO
[illegible]		[illegible]	[illegible]

EXAMINER

[illegible]

[illegible]
CHIRON CORPORATION
INTELLECTUAL PROPERTY R-440
P O BOX 8097
EMERYVILLE CA 94662-8097

ART UNIT	PAPER NUMBER
1643	10

DATE MAILED: 04/10/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 1/26/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire --3-- month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-116 is/are pending in the application.
Of the above, claim(s) 1-30+82-116 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 31-81 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U S C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U S C § 119(e)

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s) 4+7
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1643.

2. Applicant's election without traverse of Group III, claims 31-81, in Paper No. 9 is acknowledged. Claims 1-30 and 82-116 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 9.

Claim Rejections - 35 USC § 112

3. Claims 31-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31, 34-63, 80 and 81 recite the term "homologous" in reference to nucleic acid or amino acid sequences. The term "homologous" can encompass several distinct definitions, and it is not clear which of these is intended within the scope of the claim. Two sequences may be homologous in that they are evolutionarily related. These sequences may also be homologous in that they share a certain percentage of sequence similarity or sequence identity. Two sequences may also be structurally homologous, wherein the sequences may have no sequence identity, yet

form similar tertiary structures. Finally, polypeptides encoded by two sequences may have similar biological properties, i.e. be functionally homologous, without apparent sequence similarity. The specification, at pages 16 and 17, sets forth that "substantially homologous" sequences have at least 60% sequence similarity. The above rejected claims simply indicate that the sequences are homologous to other sequences, without reciting a percent similarity, or degree of similarity to a particular sequence. There is no indication in the specification as to how other homologous species are to be identified, nor exactly to what sequences the claimed nucleic acids should be homologous. The claims do not recite any information which would indicate the metes and bounds of the term homologous, and are therefore indefinite.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 31-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta.

Claims 31-63 are drawn to isolated nucleic acids of monoclonal antibodies to HCV E2 which are homologous to a variety of VH or VL sequences (SEQ ID NOs: 15-27).

Mehta (US Patent 5,308,750) discloses mouse monoclonal antibodies to HCV E2. These antibodies are extremely useful in immunoassay and other diagnostic applications. Mehta discloses the use of Fab fragments of the monoclonal antibodies. The sequences encoding the mouse monoclonal VH and VL regions, which are inherent to the antibodies of Mehta, are homologous to human monoclonal antibodies specific for HCV E2. The antibodies of Mehta are very useful, and one would be strongly motivated to sequence those same antibodies for the purposes of recombinant expression, and for purposes of identifying or creating the human equivalent of those same antibodies.

6. Claims 31-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong and Mehta, in view of Hoogenboom and Chanock.

Claims 31-81 are drawn to isolated nucleic acid sequences encoding a human Fab fragment which binds to a HCV E2 antigen, vectors and host cells comprising those sequences, and methods of producing the recombinant protein.

Hoogenboom (WO 93/06213) sets forth methods for the production of recombinant human monoclonal antibodies. These antibodies are produced by a combinatorial library

approach, and selected through immunoassays. These techniques make it possible to isolate high affinity and/or neutralizing antibodies to various viral antigens. The sequences encoding the isolated Fab fragments can then be isolated, sequences and used in various expression vectors and systems for recombinant expression of the desired human Fab.

Wong (Wong et al 1995 J Investigative Medicine 43 (2) supplement 2 p 397A) teaches that monoclonal antibodies to the E2 protein of HCV prevent penetration of the virus into its target cells. This indicates that monoclonal antibodies to the E2 protein could have significant impact on the treatment of and the prevention of HCV.

Mehta (US Patent 5,308,750) discloses mouse monoclonal antibodies to the E2 protein of HCV. Mehta discloses the usefulness and importance of these antibodies.

Chanock (Chanock et al 1993 Infectious agents and disease 2:118-131) teaches the usefulness and benefits of using the recombinant human monoclonal F(ab) fragments that have been cloned from a combinatorial library in the treatment or prevention of viral diseases.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned and identified sequences encoding human Fab fragments specific for the E2 protein of HCV from a combinatorial library through the methods of Hoogenboom and to have further cloned these sequences into appropriate expression vectors for the purposes of recombinant expression of the Fab fragments as set forth by Chanock. One would have wanted to produce these antibodies because monoclonal antibodies against the E2 protein had been shown by Wong to prevent the penetration of HCV into target cells, and Mehta disclosed that these

antibodies would be useful in immunoassays and diagnostic procedures as a more reliable indication of HCV infection.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 8:00 am and 5:30 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

mkz
April 8, 1998

MICHAEL [illegible] WOODWARD
PRIMARY EXAMINER
ART UNIT
1643